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CHEMICAL EVOLUTION AND THE ORIGIN OF LIFE

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"Ante, mare et tellus, et quod tegit omnia caelum,
Unus erat toto Naturae vultus in orbe,
Quem dixere chaos; rudis indigestaque moles;
Nec quidquam. nisi pondus iners; congestaque eodem
Non bene junctarum discordia semina rerum."

THUS wrote Ovid many centuries ago; and present-day theories are tending to the idea that life evolved in the murky dust cloud of the primitive cosmos.

The experimental approach to the question of the origin of life is the culmination of the naturalistic movement which began with the Renaissance and reached its height in the middle of the nineteenth century with the Darwinian theory of evolution. The idea of the biological unity of everything living, and the evolution of the higher forms of life from the lower—an idea which caused a revolt among the humanists of the nineteenth century—is to-day the corner stone of modern biology. If this concept of evolution is pushed to its logical conclusion, another form of evolution has to be postulated, prior to biological evolution, namely, chemical evolution.

With great insight the physicist, Tyndall, wrote in 1871: "Darwin placed at the root of life a primordial germ, from which he conceived that the amazing richness and variety of the life now upon the earth's surface might be deduced. If this hypothesis were true, it would not be final. The human imagination would infallibly look behind the germ and, however hopeless the attempt, would enquire into the history of its genesis. . . . A desire immediately arises to connect the present life of our planet with the past. We wish to know something of our remotest ancestry. . . . Does life belong to what we call matter or is it an independent principle inserted into matter at some suitable epoch, when the physical conditions became such as to permit of the development of life ?"[1].

Our difficulty is not with the quality of the problem but with its complexity. "The evolution movement", wrote Bergson, "would be a simple one, and we should soon be able to determine its direction if life had described a single course like that of a solid ball shot from a cannon. But it proceeds rather like a shell, which suddenly bursts into fragments, which fragments, being themselves shells, burst in their turn into fragments, destined to burst again, and so on for a time incommensurably long. We perceive only what is nearest to us, namely, the scattered movements of the pulverized explosions. From them we have to go back, stage by stage, to the original movement."[2] Even the formulation of this problem is perhaps beyond the reach of any one scientist, for such a scientist would have to be at the same time a competent mathematician, a physicist, and an experienced organic chemist. He should have a very extensive knowledge of geology, geophysics and geochemistry, and, besides all this, be absolutely at home in all biological disciplines. Sooner or later, this task would have to be given to groups representing all these faculties and working closely together theoretically as well as experimentally. Such was the view professed by Bernal in 1949 (ref. 3). However, to-day we have reason to be more optimistic. For the first time in human history, the sciences which arose as separate disciplines are seen fused together, and this view stretches from the beginning to the end of scientific endeavour.

In the first stage of chemical evolution, the primeval cloud of hydrogen gas by a series of reactions—implosion, fusion and fission—gave rise to the elements of the Periodic Table. This event probably occurred 20 thousand million years ago. About 15 thousand million years later, when the solar system was being formed, the highly reactive elements probably existed in their reduced form—methane, ammonia and water. When the planet Earth was being born from the primitive dust cloud, 4·5 thousand million years ago, the rudimentary molecules which were the forerunners of the complex biological polymers of 2 thousand million years later were perhaps already in existence.

In this scheme of things, life is only a special and very complicated form of the motion of matter. It arose as a new property of matter which it had not possessed earlier, and which only occurred at a particular period in the existence of our planet and resulted from its orderly development. "The origin of life was not an occurrence ascribed to some definite place and time," wrote Margolis[4], "it was a gradual process operating upon the earth over an inconceivably long span of time, a process of unfolding which consumed perhaps more millions of years than was required for the evolution of all the species of living things." A long chemical evolution was considered necessary for the origin of life. Three distinct chemical phases of this evolutionary process could be postulated; inorganic, organic chemistry and biological chemistry.

Life, then, may be considered to be an inevitable process and bound to appear in the cosmos wherever conditions are favourable. Sampling of galaxy population to the limit attainable by present telescopes shows that there are more than 10^{20} stars in the universe. Like our own

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Sun, each one of these stars can provide the energy for plant and animal life. Two factors become abundantly clear: that there is nothing unique about our Sun which is the mainstay of life on this planet, and that there are more than 10^{20} opportunities for the existence of life. If we adopt a process of restriction and suppose: that because of doubling, clustering, secondary collisions, etc., only one star in a thousand has a planetary system; that only one out of a thousand of those stars with systems of planets has one or more planets at the right distance from the star to provide the water and warmth that protoplasm requires; that of these stars only one out of a thousand has a planet large enough to hold an atmosphere; that the suitable chemical composition for life to arise occurs only once in a thousand times, only one star in 10^{12} meets the necessary rigid requirements. Even so, there are 10^{8} planetary systems suitable for life. Such was Harlow Shapley's conservative estimate[5]. Su-Shu Huang, however, has imposed less-rigid requirements and has set the upper limit of stars that actually support life as 5 per cent, that is, 10^{18} stars[6].

This conclusion which astronomers have reached by the rigorous analysis of astronomical evidence was already prophetically described by the Italian, Giordano Bruno, in the sixteenth century: "Sky, universe, all-embracing ether, and immeasurable space alive with movement . . . all these are of one nature. In space there are countless constellations, suns, and planets; we see only the suns because they give light; the planets remain invisible, for they are small and dark. There are also numberless earths circling around their suns, no worse and no less inhabited than this globe of ours. For no reasonable mind can assume that heavenly bodies which may be far more magnificent than ours would not bear upon them creatures similar or even superior to those upon our human Earth".

The search for extra-terrestrial life is the prime goal of space biology. The result of such a discovery may have an effect on human thinking far more profound than the Darwinian or Copernican revolutions. If our sallies into space should in the near future demonstrate that Martian life is a reality, and its origin independent of life on Earth a certainty, we cannot escape the conclusion that there is nothing unique about the origin of life on Earth and that the interplay of cosmic forces and matter would have given rise to a similar sequence of events in the countless number of planetary systems in the universe.

While there is a distinct possibility of our finding an answer to the question of the existence of life in our own planetary system by an inspection of the planets with our immediate or remote sensors, the only way by which we can answer the questions for systems outside our planets is by making radio contact with other civilizations in outer space. "There is one race of men; one race of gods; both have breath of life from a single mother. But sundered power holds us divided, so that one is nothing, while for the other the brazen sky is established their sure citadel forever", wrote Pindar in the sixth *Nemean Ode*.

However, we have the possibility of an experimental approach to the problem. As the laws of chemistry and physics are universal, the retracing of the stages by which life appeared on Earth would give strong support to the theory of its existence elsewhere in the universe. Laboratory experiments on Earth can reveal which materials and conditions available in the universe might give rise to the basic chemical components of living systems—nucleic acids and proteins. Experiments may even reveal how the transition from chemicals to the orderliness of living systems may have occurred.

The idea of life arising from non-life, or the theory of spontaneous generation, had been accepted for centuries. One had only to accept the evidence of the senses, thought the ancients: worms from mud, maggots from decaying meat, and mice from old linen. The ancient Egyptians believed in this. Recall *Anthony and Cleopatra*, Act II, Scene VII, where Lepidus tells Mark Anthony, "Your serpent of Egypt is bred . . . now of your mud by the operation of our sun—so is your crocodile". Aristotle had taught the same doctrine in his *Metaphysics*. Newton, Harvey, Descartes, van Helmont, all accepted this without serious question. Even the English Jesuit, John Tuberville Needham, could subscribe to this view, for *Genesis* tells not that God created plants and animals directly but that he bade the earth and waters to bring them forth: "And God said let the earth bring forth grass, the herb yield seed and the fruit tree yielding fruit. . . . Let the waters bring forth abundantly the moving creature that hath life . . .".

Pasteur's rigorous experimentation outlawed the theory of spontaneous generation, which was based on incompetent observation and the willingness to accept the superficial evidence of the senses. The story of Louis Pasteur is often told to beginning students in biology as a triumph of reason over mysticism. But to-day we have evidence for the contrary. The reasonable view may be to believe in spontaneous generation though in a restricted and a logical sense.

Charles Darwin was a pioneer in the speculation on the early conditions for the origin of life. In a letter to a friend he wrote: "But if [and oh what a big if !] we could conceive in some warm little pond, with all sorts of ammonia and phosphoric salts, light, heat, electricity, etc., present that a protein compound was chemically formed ready to undergo still more complex changes"[7]. Darwin's own thinking could perhaps be traced to the influence of his grandfather Erasmus Darwin who more than half a century earlier had written that "all vegetables and animals now existing were originally derived from the smallest microscopic ones formed by spontaneous vitality"[8]. This was too outrageous a declaration for the conservative thinking of Darwin's contemporaries. At the height of the controversy over the origin of the species, little or no attention was paid to the remote question of the origin of life.

The great impetus, however, to the experimental investigation of the origin of life began with the Russian biochemist, Oparin. Already in 1924 a preliminary booklet was published by him in Russian pointing out that ". . . there was no fundamental difference between a living organism and lifeless matter. The complex combination of manifestations and properties so characteristic of life must have arisen in the process of the evolution of matter". Thirteen years later, he published his book *On the Origin of Life*[9]. This book has gone through three editions and is the classic on the subject.

According to Oparin: "At first there were the simple solutions of organic substances, the behaviour of which was governed by the properties of their component atoms and the arrangement of those atoms in the molecular structure. But gradually as a result of growth and increased complexity of the molecules new properties have come into being and a new colloidal-chemical order was imposed on the more simple organic chemical relations. These newer properties were determined by the spatial arrangement and mutual relationship of the molecules. Even this configuration of organic matter was still insufficient to give rise to primary living things. For this, the colloidal systems in the process of their evolution had to acquire properties of a still higher order, which would permit the attainment of the next and more advanced phase in the organization of matter. In this process biological orderliness already comes into prominence. Competitive speed of growth, struggle for existence and, finally, natural selection determined such a form of material organization which is characteristic of living things of the present time".

Independently of Oparin, Haldane had speculated on the early conditions suitable for the emergence of terrestrial life[10]. "Now, when ultra-violet light acts on a mixture of water, carbon dioxide, and ammonia, a vast variety of organic substances are made, including sugars, and apparently some of the materials from which proteins are built up. . . . Before the origin of life they must have accumulated till the primitive oceans reached the constituency of *hot dilute soup*. To-day an organism must trust to luck, skill, or strength to obtain its food. The first precursors of life found food available in considerable quantities, and had no competitors in the struggle for existence. As the primitive atmosphere contained little or no oxygen, they must have obtained the energy they needed for growth by some process other than oxidation—in fact, by fermentation. For, as Pasteur put it, fermentation is life without oxygen".

Twenty years after the appearance of Haldane's paper in the *Rationalist Annual*, J. D. Bernal of the University of London theorized before the (British) Physical Society in a lecture entitled "The Physical Basis of Life"[3]: "Condensations and dehydrogenations are bound to lead to increasingly unsaturated substances, and ultimately to simple and possibly even to condensed ring structures, almost certainly containing nitrogen, such as the pyrimidines and purines. The appearance of such molecules makes possible still further syntheses. The primary difficulty, however, of imagining processes going thus far is the extreme dilution of the system if it is supposed to take place in the free ocean. The concentration of products is an absolute necessity for any further evolution. One method of concentration would, of course, take place in lagoons and pools which are found to have fringed all early coastlines, produced by the same physical factors of wind and wave that produce them to-day. It has occurred to me, however, that a much more favourable condition for concentration, and one which must certainly have taken place on a very large scale, is that of absorption in fine clay deposits, marine and fresh water. Our recent knowledge of the structures of clays has shown what an enormous role they still play in living processes. There is probably to-day more living matter, that is protein, in the soil and in the estuarine and sea-bed clays than above the surface or in the waters. It has already been shown that organic chemicals of a wide variety are preferentially absorbed on such surfaces in a regular way. It is therefore certain that the primary photochemical products would be so absorbed, and during the movement of the clay might easily be held blocked from further possibly destructive transformations. In this way relatively large concentrations of molecules could be formed".

Among the first experiments designed to test some of the theories of the origin of life were those of Calvin and his associates, who, in 1951, irradiated water and carbon dioxide and obtained significant yields of formaldehyde and formic acid[11]. In 1953, Stanley Miller, then a graduate student in Harold Urey's laboratory, assembled a sample of the assumed primeval terrestrial atmosphere, consisting of methane, ammonia, water-vapour and hydrogen, and exposed it to an electric discharge, simulating lightning. Amino-acids and other organic compounds found in living systems were formed[12].

Since this classical experiment, several investigators have entered this field. Notable among them are Sidney Fox of Florida State University[13], and John Oro of the

University of Houston[14]. The majority of publications have dealt with the formation of amino-acids and the nucleic acid constituents, from a wide variety of conditions which may be considered pre-biological. Fox's work has centred around the origin of proteins. A plausible answer seems to have begun to take shape. Proteinoids have been obtained by the thermal polymerization of the 18 amino-acids. These proteinoids have a distinct tendency to form microspheres having diameters in a bacterial range. Starting with ammonium cyanide, Oro has synthesized adenine and a number of biochemical intermediates of purines.

In our own laboratory, we have initiated a programme of research using the various forms of energy which were known to have existed in the primitive Earth. The constituents of the atmosphere of the primordial Earth are being exposed to ultra-violet light, electric discharges, ionizing radiation and heat. Tesla coils supply the lightning, germicidal tubes the ultra-violet light, the electron beam of the linear accelerator at the University of California, Berkeley, gives us our β-particles. The reaction products are being analysed for amino-acids, purines, pyrimidines, etc. An attempt is being made to polymerize these single units to produce the large molecules similar to the replicating systems we know to-day.

The results we have obtained so far are indeed very encouraging. Starting with the primitive atmospheres, we have been able to synthesize several constituents of the nucleic acid molecule—the purines, adenine and guanine, the sugars ribose and deoxyribose, the nucleoside adenosine and the nucleotide adenylic acid. Under similar possible primitive Earth conditions, adenosine triphosphate (ATP) appears to be formed in appreciable yield. Published results from several laboratories thus demonstrate that the first and second stages of chemical evolution, namely, the inorganic and organic, can be satisfactorily retraced in the laboratory.

We are optimistic that the path of chemical evolution will be outlined in the laboratory. The biochemical knowledge which has been amassed within a few years has given us a deep insight into some of Nature's most secret processes. With this understanding to help us, the time needed to solve our problem may not be long. We cannot deny the immensity of the prospect for any man's philosophical position or shrink from its pursuit on account of the difficulty of the task.

More than 500 years ago, Copernicus, in *De Revolutionibus Orbium Coelestium* reversed the scientific thinking of his time about man's place in the physical universe. A hundred years ago, Darwin's theory of evolution destroyed age-old beliefs of the uniqueness of man by tracing his origin from the brute. To-day, we are gradually learning to accept the Oparin–Haldane hypothesis that life is only a special and complicated property of matter and that *au fond* there is no difference between a living organism and lifeless matter.

To conclude with Harlow Shapley: "The new discoveries and developments contribute to the unfolding of a magnificent universe; . . . With our confrères on distant planets; with our fellow animals and plants of land, air and sea; with the rocks and waters of all planetary crusts, and the photons and atoms that make up the stars—with all these we are associated in an existence and an evolution. . . . And as groping philosophers and scientists we are thankful for the mysteries that still lie beyond our grasp".

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